UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/655,873	09/05/2003	Shyam S. Mohapatra	USF-182XC1	6872

23557 7590 06/26/2008

SALIWANCHIK LLOYD & SALIWANCHIK
A PROFESSIONAL ASSOCIATION
PO BOX 142950
GAINESVILLE, FL 32614-2950

EXAMINER	
NOBLE, MARCIA STEPHENS	
ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
06/26/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/655,873	MOHAPATRA ET AL.	
	Examiner	Art Unit	
	MARCIA S. NOBLE	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,6-9,12,15,18,19,43,45-50,52,53,58,60,62,64,66 and 71-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *43,45-50,52,64, 71, and 72* is/are allowed.

6)☒ Claim(s) *53,58,62 and 73* is/are rejected.

7)☒ Claim(s) *1, 3, 6-9, 12, 15, 18, 19, 58, 60, 66, 73, and 74* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/2007 has been entered.

Status of Claims

2. Claims 1, 3, 6-9, 12, 15, 18, 19, 43, 45-50, 52, 53, 58, 60, 62, 64, 66, and 71-75 are pending. Claims 1, 18, 43, 58, 60, 62, 64, and 66 are amended, claims 2, 4, 11, 14, 20, 21, 23-31, 44, 54-57, 59, 61, 63, 65, and 67-70 are cancelled, and claims 74 and 75 are newly added by the amendment, filed 10/31/2007. Claims 1, 3, 6-9, 12, 15, 18, 19, 43, 45-50, 52, 53, 58, 60, 62, 64, 66, and 71-75 are under consideration.

Withdrawn Rejections

3. The rejection of claims 54-57, 69, and 70, under 35 U.S.C. 103(a) as being unpatentable over Hogan et al. {Hogan et al. (1998) Eur. J. Immunol. 28: 413-423}, and further in view of Li et al. {Li. et al. (1996) J. Immunol. 157: 3216-3219} and further in view of US patent 6,693,086 (2.17.2004) priority to (6.25.1998), hereafter referred to as

Dow et al, and O'Donnell et al. {O'Donnell (1999) J. Immunol. 163:4246-4252}, as set forth in the Office Action, mailed 6/5/2006 on pages 4-6, is withdrawn.

The rejection of claims 1, 3, 6-9, 11, 12, 15, 18, 19, 43, 45-50, 52, 54-57, 60, 64, 66, and 68-72, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method of modulating an immune response comprising administering by intramuscular injection to a patient an effective amount of pharmaceutical composition comprising a nucleic acid encoding the nucleic acid sequence of SEQ ID NO:7, which encodes the p35 subunit of human IL-12, and the nucleic acid sequence of SEQ ID NO:9, which encodes the p40 subunit of human IL-12 both operably linked to a promoter capable of driving expression of said nucleic acid and the nucleic acid sequence of SEQ ID NO:11, which encodes human IFN-γ, operably linked to a promoter capable of driving expression of said nucleic acid, and administering an antigen subcutaneously, wherein the administration of said composition and said antigen results in an increase of Th1-type cytokines INF-γ and IL-2, an increase in the levels of IGg2a specific to said antigen, a decrease of Th2-type cytokine IL-2, and reduced serum IgE levels;

does not reasonably provide enablement for:

A method comprising administering 1) any nucleic acid sequence encoding IL-12, a promoter operably linked to any nucleic acid or protein, any nucleic acid sequence encoding any IFN-γ, a promoter operably linked to any nucleic acid or protein, and an antigen, 2) administering by any route of administration, 3) administering the two nucleic

acids independently, wherein the administering step involves a selection step, 4) and wherein the administration results in an increase in any or all Th1-type cytokine production, an increase in any or all IgG2a, a decrease in any or all Th2-type cytokine production, and a decrease in IgE levels; as set forth in the Office Action, mailed 2/26/2007 on pages 8-16, is withdrawn.

Claim Objections

4. Claim 1 is objected to because of the following informalities: Claim 1, line 9, recites "production production". Remove one of the recitations of "production". Appropriate correction is required.

Claims 3, 6-9, 12, 15, 18, 19, 58, 60, 66, 73, and 74 are dependent upon claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The scope of enablement rejection set for in the Office Action, mailed 2/26/2007, has been modified as follows:

5. Claims 53, 58, 62, and 73 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of modulating an immune response comprising co-administering to a mammal: an effective amount of a nucleic acid or plasmid comprising a nucleic acid sequence encoding p35 and p40 subunits of human IL-12 operably linked to a promoter; an effective amount of a nucleic acid or plasmid comprising a nucleic acid sequence encoding IFN-gamma operably linked to a promoter; and an antigen, such that the co-administering results in an increase of IFN-gamma and IL-2 production, an increase in IgGa specific to the antigen, a decrease of IL-4 production, and reduced serum IgE, wherein the nucleic acid or plasmid are administered by a route selected from the group consisting of intramuscularly and intranasally, does not reasonably provide enablement for the claimed method, wherein the nucleic acid or plasmid are administered by an oral route or through a mucosal route. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

The instant enablement rejection is being made for claims 53, 58, 62, and 73 because neither the specification nor the art provide predictable specific guidance to implement the specific embodiments of these claims.

Applicant's arguments filed 10/31/2007 have been fully considered but they are not fully persuasive. Applicant traverses the original rejection on the grounds that Applicant need not disclose every route of administration in the specification (p. 9, line 11 of remarks). Applicant asserts that the specification teaches intramuscular and

subcutaneous injection and also incorporates US Patent No. 6, 489,306 by reference which teaches an intranasal administration (p. 9, lines 7-11 of remarks). Applicant also asserts that the art discloses intradermal, intravenous, and other routes of administration that will work in immunotherapy (p. 9, lines 11-19 or remarks).

Applicant's arguments have only been found to be partially persuasive. The scope of enablement has been modified to incorporate intranasal administration as well as intramuscular administration. Similarly claim 1 has been removed from the original rejection, which does not specify the route of administration, because several means of administration are enabled by the specification and the art.

However, claims 53 and 73 claim an oral route of administration and claims 58 and 62 claim a mucosal route of administration. The art teaches that oral and mucosal routes of administration are highly unpredictable. The post-filing art of Kai and Ochiya (Pharm Res 21(5):838-843, 2004) teach, "Oral delivery of the DNA, though possessing certain obvious advantages, remains problematic due to the acidic environment of the stomach. Therefore, proper methods of protecting the DNA during its delivery to the target organ must be found." (See p. 841, col 1, last par, lines 5-8.) Kai and Ochiya teach that chitosan complex to DNA is one possible means of delivery, but further discloses that chitosan is not a suitable carrier because it is soluble in an acidic environment, as is the case of the stomach (p. 838, col 2, par 3, line 1-2, and p. 841, col 2, par 1, lines 2-8). Kai and Ochiya teach that "even if delivery of a chitosan/DNA complex to the intestine were possible, it would still be difficult to transport the genes across mucosal epithelium." (p. 838, col 2, par 3, lines 8-10). Therefore because of the

problematic nature of the acidic stomach environment which destroy DNA vectors, as taught by Kai and Ochiya, oral deliveries are highly unpredictable. Similarly, because of the problematic nature of traversal of a DNA vector across the mucosal epithelial barrier, as taught by Kai and Ochiya, mucosal routes of administration are also unpredictable.

In the face of an unpredictable art, such as in the case of an oral and mucosal route of administration, an artisan would look to the specification for specific guidance to overcome the unpredictabilities taught in the art. However, the specification fails to provide specific guidance to teach an oral or mucosal route of administration. Therefore, the instant claims that recite the use of an oral or mucosal route of administration are not enable by the specification or art.

Although Applicant is correct in their assertion that the specification need not teach every route of administration. However, in the present set of claims, applicant is claiming specific routes of administration known in the art at the time of filing to be unpredictable and without routine experimentation. Thus, if the art is considered unpredictable, as is the case with an oral and mucosal administration, the specification must provide specific guidance that teaches a means to overcome the unpredictabilities. In the instant case, the art of oral and mucosal administration are unpredictable, and therefore the specification needs to provide guidance for a predictable means of oral and mucosal administration. The specification lacks such guidance. Therefore, Applicant's argument is not found persuasive.

Therefore, because neither the art nor the specification provide specific guidance to predictably teach a means of oral and mucosal administration that would not require undue experimentation, instant claims 53, 58, 62, and 73 drawn to the use of an oral or mucosal administration are not enabled.

Conclusions

6. Claim 1 is objected to. Claims 3, 6-9, 12, 15, 18, 19, 58, 60, 66, 73, and 74 are dependent upon claim 1. When claim 1 is amended and no longer objected to, claim 1 and the above listed dependent claims may be allowable. Claims 53, 58, 62, and 73 are rejected. Claims 43, 45-50, 52, 64, 71, and 72 appear to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCIA S. NOBLE whose telephone number is (571)272-5545. The examiner can normally be reached on M-F 9 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch, Ph.D./
Primary Examiner, Art Unit 1632

Marcia S. Noble
AU 1632